[COMMITTEE PRINT]

[SHOWING TEXT OF COMMITTEE PRINT AS APPROVED BY SUBCOMMITTEE ON HEALTH ON JUNE 19, 2007]

110TH CONGRESS
1ST SESSION

H. R. _____

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric research improvement, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

M__. _____ introduced the following bill; which was referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to pediatric research improvement, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Pediatric Research Equity Act of 2007''.

SEC. 2. REAUTHORIZATION OF PEDIATRIC RESEARCH EQUITY ACT.

Section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) is amended to read as follows:

"SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.

''(a) NEW DRUGS AND BIOLOGICAL PRODUCTS.—

''(1) IN GENERAL.—A person that submits, on or after the date of enactment of the Pediatric Research Equity Act of 2007, an application (or supplement to an application)—

''(A) under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration; or

''(B) under section 351 of the Public Health Service Act (42 U.S.C. 262) for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration; shall submit with the application the assessments described in paragraph (2).

''(2) ASSESSMENTS.—

''(A) IN GENERAL.—The assessments referred to in paragraph (1) shall contain data, gathered using appropriate formulations for

each age group for which the assessment is required, that are adequate—

"(i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and

"(ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

"(B) SIMILAR COURSE OF DISEASE OR SIMILAR EFFECT OF DRUG OR BIOLOGICAL PRODUCT.—

"(i) IN GENERAL.—If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

"(ii) EXTRAPOLATION BETWEEN AGE GROUPS.—A study may not be needed in each pediatric age group if data from one

age group can be extrapolated to another age group.

''(iii) INFORMATION ON EXTRAPOLATION.—A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in the medical review that is collected as part of the application under section 505 of this Act or section 351 of the Public Health Service Act (42 U.S.C. 262).

''(3) DEFERRAL.—

''(A) IN GENERAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1) until a specified date after approval of the drug or issuance of the license for a biological product if—

''(i) the Secretary finds that—

''(I) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;

''(II) pediatric studies should be delayed until additional safety or ef-

fectiveness data have been collected; or

''(III) there is another appropriate reason for deferral; and

''(ii) the applicant submits to the Secretary—

''(I) certification of the grounds for deferring the assessments;

''(II) a description of the planned or ongoing studies;

''(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; and

''(IV) a timeline for the completion of such studies.

''(B) ANNUAL REVIEW.—

''(i) IN GENERAL.—On an annual basis following the approval of a deferral under subparagraph (A), the applicant shall submit to the Secretary the following information:

''(I) Information detailing the progress made in conducting pediatric studies.

''(II) If no progress has been made in conducting such studies, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time.

''(ii) PUBLIC AVAILABILITY.—The information submitted through the annual review under clause (I) shall promptly be made available to the public in an easily accessible manner, including through the website of the Food and Drug Administration.

''(4) WAIVERS.—

''(A) FULL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection if the applicant certifies and the Secretary finds that—

''(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed);

"(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups; or

"(iii) The drug or biological product—

"(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

"(II) is not likely to be used in a substantial number of pediatric patients.

"(B) PARTIAL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the secretary finds that—

"(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

"(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

"(iii) the drug or biological product—

"(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

"(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

"(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

"(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the ap-

plicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the website of the Food and Drug Administration.

''(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

''(b) MARKETED DRUGS AND BIOLOGICAL PRODUCTS.—

''(1) IN GENERAL.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, after providing notice in the form of a letter and an opportunity for written response and a meeting, which may include an advisory committee meeting, the Secretary may (by order in the form of a letter) require the sponsor or holder of an approved application for a drug under section 505 or the holder of a license for a biological product under section 351 of the Public Health Service Act (42 U.S.C. 262) to submit by a specified date the assessments

described in subsection (a)(2), if the Secretary finds that—

''(A)(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

''(ii) adequate pediatric labeling could confer a benefit on pediatric patients;

''(B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for 1 or more of the claimed indications; or

''(C) the absence of adequate pediatric labeling could pose a risk to pediatric patients.

''(2) WAIVERS.—

''(A) FULL WAIVER.—At the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that—

''(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or

''(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

''(B) PARTIAL WAIVER.—At the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

''(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

''(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

''(iii)(I) the drug or biological product—

''(aa) does not represent a meaningful therapeutic benefit over existing

therapies for pediatric patients in that age group; and

''(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

''(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

''(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

''(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the website of the Food and Drug Administration.

''(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

''(c) MEANINGFUL THERAPEUTIC BENEFIT.—For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B)(I) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary determines that—

''(1) if approved, the drug or biological product could represent an improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

''(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

''(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit an assessment described in subsection (a)(2), or a request for approval of a pediatric formulation

described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b)—

''(1) the drug or biological product that is the subject of the assessment or request may be considered misbranded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 303); but

''(2) the failure to submit the assessment or request shall not be the basis for a proceeding—

''(A) to withdraw approval for a drug under section 505(e); or

''(B) to revoke the license for a biological product under section 351 of the Public Health Service Act (42 U.S.C. 262).

''(e) MEETINGS.—Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

''(1) information that the sponsor submits on plans and timelines for pediatric studies; or

''(2) any planned request by the sponsor for waiver or deferral of pediatric studies.

''(f) REVIEW OF PEDIATRIC ASSESSMENTS, DEFERRALS, AND WAIVERS.—

''(1) REVIEW.—The Secretary shall utilize an internal committee to review all determinations that a pediatric assessment is required under this section and all deferral and waiver requests made pursuant to this section. Such internal committee shall include, as appropriate, employees of the Food and Drug Administration, with expertise such as pediatrics (including representation from the Office of Pediatric Therapeutics), biopharmacology, statistics, chemistry, legal issues, pediatric ethics, subject matter expertise pertaining to the pediatric product under review, and other individuals as determined appropriate by the Secretary.

''(2) ACTIVITY BY COMMITTEE.—The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

''(3) DOCUMENTATION OF COMMITTEE ACTION.—For each drug or biological product, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (4), which members of the committee participated in such activity.

''(4) REVIEW OF REQUESTS FOR PEDIATRIC ASSESSMENTS, DEFERRALS AND WAIVERS.—All deter-

minations that a pediatric assessment required under this section and all requests for deferrals and waivers from the requirement to conduct a pediatric assessment under this section shall be reviewed by the committee referred to in paragraph (1).

''(5) TRACKING OF ASSESSMENTS AND LABELING CHANGES.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall track and make available to the public in an easily accessible manner, including through post on the website of the Food and Drug Administration—

''(A) the number of assessments conducted under this section;

''(B) the specific drugs and biological products and their uses assessed under this section;

''(C) the types of assessments conducted under this section, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

''(D) the total number of deferrals requested and granted under this section and, if granted, the reasons for such deferrals, the timeline for completion, and the number com-

pleted and pending by the specified date, as outlined in subsection (a)(3);

"(E) the number of waivers requested and granted under this section and, if granted, the reasons for the waivers;

"(F) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons any such formulation were not developed;

"(G) the labeling changes made as a result of assessments conducted under this section;

"(H) an annual summary of labeling changes made as a result of assessments conducted under this section for distribution pursuant to subsection (h)(2); and

"(I) an annual summary of information submitted pursuant to subsection (a)(3)(B).

"(6) COMMITTEE.—The committee established under paragraph (1) is the committee established under section 505A(f)(1).

"(g) LABELING CHANGES.—

"(1) PRIORITY STATUS FOR PEDIATRIC APPLICATIONS.—Any supplement to an application under section 505 and section 351 of the Public Health Service Act proposing a labeling change as a result

of any pediatric assessments conducted pursuant to this section—

"(A) shall be considered a priority application or supplement; and

"(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

"(2) DISPUTE RESOLUTION.—

"(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If, on or after the date of enactment of the Pediatric Research Equity Act of 2007, the Commissioner determines that a sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application or supplement, not later than 180 days after the date of the submission of the application or supplement—

"(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

"(ii) if the sponsor does not agree within 30 days after the Commissioner's request to make a labeling change re-

quested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

''(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

''(i) review the pediatric study reports; and

''(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

''(C) CONSIDERATION OF RECOMMENDATIONS.—The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling changes that the Commissioner determines to be appropriate.

''(D) MISBRANDING.—If the sponsor of the application, within 30 days after receiving a request under subparagraph (c), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the

drug that is the subject of the application to be misbranded.

''(E) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under this Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

''(3) OTHER LABELING CHANGES.—If the Secretary makes a determination that a pediatric assessment conducted under this section does or does not demonstrate that the drug that is the subject of such assessment is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary shall order the label of such product to include information about the results of the assessment and a statement of the Secretary's determination.

''(h) DISSEMINATION OF PEDIATRIC INFORMATION.—

''(1) IN GENERAL.—Not later than 180 days after the date of submission of a pediatric assessment under this section, the Secretary shall make available to the public in an easily accessible manner the medical, statistical, and clinical pharmacology reviews of such pediatric assessments, and shall post such assessments on the website of the Food and Drug Administration.

''(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall require that the sponsors of the assessments that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(5)(H) distribute such information to physicians and other health care providers.

''(3) EFFECT OF SUBSECTION.—Nothing in this subsection shall alter or amend Section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

''(i) ADVERSE EVENT REPORTING.—

''(1) REPORTING IN YEAR ONE.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, during the one-year period begin-

ning on the date a labeling change is made pursuant to subsection (g), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics. In considering the report, the Director of such Office shall provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this Act in response to such report.

''(2) REPORTING IN SUBSEQUENT YEARS.—Following the one-year period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering the report, the Director of such Office may provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such report.

''(3) EFFECT.—The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

''(j) SCOPE OF AUTHORITY.—Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

''(k) ORPHAN DRUGS.—Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under section 526.

''(l) INSTITUTE OF MEDICINE STUDY.—

''(1) IN GENERAL.—Not later than three years after the date of the enactment of the Pediatric Research Equity Act of 2007, the Secretary shall contract with the Institute of Medicine to conduct a study and report to Congress regarding the pediatric studies conducted pursuant to this section since 1997.

''(2) CONTENT OF STUDY.—The study under paragraph (1) shall review and assess the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, the number and type of pediatric adverse events, and ethical issues in pediatric clinical trials.

''(3) REPRESENTATIVE SAMPLE.—The Institute of Medicine may devise an appropriate mechanism to review a representative sample of studies conducted pursuant to this section from each review division within the Center for Drug Evaluation and Research in order to make the requested assessment.''.

SEC. 3. GOVERNMENT ACCOUNTABILITY OFFICE REPORT.

Not later than September 1, 2011, the Comptroller General of the United States, in consultation with the Secretary of Health and Human Services, shall submit to the Congress a report that addresses the effectiveness of sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) and section 409I of the Public Health Service Act (42 U.S.C. 284m) in ensuring that medicines used by children are tested and properly labeled. Such report shall include—

(1) the number and importance of drugs and biological products for children that are being tested as a result of the amendments made by this Act and the importance for children, health care providers, parents, and others of labeling changes made as a result of such testing;

(2) the number and importance of drugs and biological products for children that are not being tested for their use notwithstanding the provisions of

this Act and possible reasons for the lack of testing, including whether the number of written requests declined by sponsors or holders of drugs subject to section 505A(g)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(g)(2)) has increased or decreased as a result of the amendments made by this Act;

(3) the number of drugs and biological products for which testing is being done and labeling changes required, including the date labeling changes are made and which labeling changes required the use of the dispute resolution process established pursuant to the amendments made by this Act, together with a description of the outcomes of such process, including a description of the disputes and the recommendations of the Pediatric Advisory Committee;

(4) any recommendations for modifications to the programs established under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) and section 409I of the Public Health Service Act (42 U.S.C. 284m) that the Secretary determines to be appropriate, including a detailed rationale for each recommendation;

(5)(A) the efforts made by the Secretary to increase the number of studies conducted in the neonate population; and

(B) the results of those efforts, including efforts made to encourage the conduct of appropriate studies in neonates by companies with products that have sufficient safety and other information to make the conduct of the studies ethical and safe; and

(6) pediatric studies conducted pursuant to this section since 1997 and labeling changes made as a result of such studies.